REMARKS

Claims 3-5 and 11-14 are pending in the subject application. No claim has been added, canceled, or amended herein. Accordingly, claims 3-5 and 11-14 are still pending and under examination.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 3-5 and 11-14 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not enable a method for preventing exaggerated restenosis in a diabetic subject by administering to the subject any sRAGE polypeptide other than murine sRAGE in vivo.

Specifically, the Examiner alleges that no detailed information for the structural feature of sRAGE that contributes to preventing exaggerated restenosis has been provided, and that one skilled in the art would not know whether sRAGE derived from different organisms would have the same biological function as mouse sRAGE.

In response, applicants respectfully traverse.

Claim 3, and dependent claims 4, 5 and 11-14, provide a method for preventing exaggerated restenosis in a diabetic subject at risk of developing exaggerated restenosis which comprises administering to the subject a therapeutically effective amount of soluble receptor for advanced glycation endproducts (sRAGE) so as to prevent exaggerated restenosis in the subject.

For a claim to be enabled, it is necessary that one skilled in the

art at the time of filing could practice the claimed invention in view of the specification without undue experimentation. In the event some experimentation were required to practice the invention, which applicants do not concede, the need for such experimentation does not by itself constitute a lack of enablement. Rather, for that to happen, the experimentation must be undue.

Applicants maintain that they have provided a representative number of embodiments of sRAGE to enable the pending claims. For example, applicants provide both DNA and amino acid sequences for murine, bovine and human RAGE, and note that RAGE sequences for other species are known (specification at pages 13-19). It is unnecessary for applicants to further provide discussion of specific structural features responsible for sRAGE function, so long as the meaning of sRAGE (i.e., the extracellular ligand-binding domain of the receptor) is clear (see, e.g., page 31, lines 8-9 of the specification).

In support of his position, the Examiner asserts that it is known in the art that the same stretch of an amino acid sequence can contribute to different biological functions in different proteins. Applicants understand the Examiner's assertion as based on the notion of alternate splicing, whereby a single polypeptide chain, depending on how it is cleaved, can give rise to different proteins having different functions. Applicants note that this notion has been misapplied here. Rather, the relevant question here is whether sRAGE in mammals other than mouse, i.e., sRAGE homologs, would be expected to behave in the same manner. They would. sRAGE homologs are not the same as splice variants, and the Examiner has not shown any reference teaching that sRAGE from one species would

be expected to behave differently than sRAGE from another species.

The Examiner further rejected claim 4 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not enable a method for preventing exaggerated restenosis in a diabetic human subject by administering to the subject any sRAGE polypeptide in vivo.

Specifically, the Examiner notes the declaration from Dr. Ann Marie Schmidt which states, in part, that the fatty Zucker rats used in the subject application is a well-established model for Type II diabetes and that the arteries of the fatty Zucker rat are diseased and its response to carotid balloon injury parallels the results observed in diabetic human subjects. However, according to the Examiner, one cannot extrapolate success in preventing exaggerated restenosis in fatty Zucker rats into success in a diabetic human subject. The Examiner further references Park, et al. which states that "no single model has yet been shown to reliably predict restenosis in humans."

In response to the Examiner's rejection of claim 4, applicants respectfully traverse.

Claim 4 provides a method for preventing exaggerated restenosis in a diabetic human subject at risk of developing exaggerated restenosis which comprises administering to the subject a therapeutically effective amount of soluble receptor for advanced glycation endproducts (sRAGE) so as to prevent exaggerated restenosis in the subject.

First, applicants note that Muller, et al., Reilly, et al. and Lafont, et al., cited earlier in support of the Examiner's position, discuss rat models having *disease-free* arteries. In contrast, the claimed method is for treating a human having diseased arteries. The fatty Zucker rat used as an experimental model in this application, and discussed in the Schmidt declaration, also has *diseased* arteries.

Second, regarding the portion of the Park, et al. reference discussing "Study Limitations", applicants understand the authors merely to be exercising an abundance of scholarly caution. That is, by their brief cautionary remarks, they merely avoid conclusively stating that the fatty Zucker rat model reflects *all* pathophysiological characteristics observed in diabetic human subjects. However, such a complete scientific showing is not necessary for the purposes of establishing the usefulness of an animal model for enablement purposes. Applicants note, based on the evidence of record, that the fatty Zucker rat is a well-established model of type I diabetes, and that one skilled in the art would understand that experimental results observed in the fatty Zucker rat would reasonably represent experimental results expected to be observed in diabetic human subjects.

In view of the above, applicants maintain that claims 3-5 and 11-14 are enabled and satisfy the requirements of 35 U.S.C. §112, first paragraph.

Summary

For the reasons set forth hereinabove, applicants maintain that the

claims pending are in condition for allowance, and respectfully request allowance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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